



Prenatal exposure to heat and humidity and infant birth size in Ghana

Aalekhya Reddam^{a,*}, Mohammed Nuhu Mujtaba^b, Cascade Tuholske^{c,d}, Seyram Kaali^b, Kenneth Ayuurebobi Ae-Ngibise^b, Blair J. Wylie^{a,e}, Danielle N. Medgyesi^a, Ellen Boamah-Kaali^b, Andrea A. Baccarelli^a, Oscar Agyei^b, Steve N. Chillrud^f, Kwaku Poku Asante^b, Darby W. Jack^a, Alison G. Lee^{g,1}, Sulemana Watara Abubakari^{b,1}

^a Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY, United States

^b Kintampo Health Research Centre, Research and Development Division, Ghana Health Service, Kintampo, Ghana

^c Department of Earth Sciences, Montana State University, Bozeman, MT, United States

^d Geospatial Core Facility, Montana State University, Bozeman, MT, United States

^e Department of Obstetrics and Gynecology, Columbia University Irving Medical Center, New York, NY, United States

^f Lamont-Doherty Earth Observatory of Columbia University, Palisades, NY, United States

^g Division of Pulmonary, Critical Care and Sleep Medicine, Icahn School of Medicine at Mount Sinai, New York, United States

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ABSTRACT

Previous studies – primarily in high income countries – have shown that high prenatal temperatures are associated with adverse birth outcomes. However, these studies are mostly focused on average exposure across the full gestational period or short-term exposure immediately prior to delivery and may miss important sensitive windows of exposure *in utero*. Further, nearly all use ambient air temperature data, which neglect physiologically important interactions between air temperature and humidity. The Ghana Randomized Air Pollution and Health Study (GRAPHS) recruited pregnant individuals from 2013 to 2015 from communities in the Kintampo North Municipality and Kintampo South District of Ghana. We estimated daily maximum shaded wet bulb globe temperature (WBG Tmax) and heat index (HI max) during pregnancy and examined associations with birth weight, birth length, head circumference, and incidence of low birth weight, preterm birth, and small for gestational age.

Using linear regression analyses, trimester average models identified that higher WBG Tmax in the first trimester was associated with larger head circumference; second trimester was associated with shorter birth length, lower birth weight and higher odds of preterm birth, and third trimester was associated with shorter gestational age and larger head circumference. Time-varying analyses using distributed lag nonlinear models find that, compared to the median, lower WBG Tmax and HI max (25th percentile) during the first half of pregnancy was associated with higher birth weight and longer birth length. Compared to the median, lower WBG Tmax and HI max (25th percentile) in the second half of pregnancy was associated with smaller head circumference while higher wet bulb globe temperature (75th percentile) was associated with larger head circumference. Overall, our study identified that higher WBG Tmax and HI max are associated with pregnancy duration and newborn size. Given the overall trend in our study area of rising temperatures, these data suggest that adaptation strategies are urgently needed to protect child health.

1. Background

Climate change is and will continue to result in higher humid-heat exposures, particularly for the poorest communities worldwide who have contributed least greenhouse emissions. Worldwide, annual

temperatures have continued to increase, with 2014–2022 being the nine warmest years on record (NOAA, 2023). Higher temperatures are associated with adverse human health outcomes such as increased all-cause mortality, cardiovascular and respiratory diseases-related mortality, and mental health issues (Liu et al., 2022; Ebi et al., 2021;

* Corresponding author.

E-mail address: aalekhya425@gmail.com (A. Reddam).

¹ Denotes equal contribution.

Arbuthnott and Hajat, 2017). Less is known about the impacts of humid-heat exposures on pregnancy, which may be a particularly vulnerable period with intergenerational health impacts (Strand et al., 2011; Samuels et al., 2022). Data from low- and middle-income countries (LMICs) on the health sensitivities of humid-heat exposures over pregnancy is urgently needed to inform public health adaptation strategies and to guide emissions mitigation strategies.

Previous studies from high-income countries have reported associations between higher temperatures during the prenatal period and adverse birth outcomes such as preterm birth, low birth weight, and increased incidence of stillbirth (Basu et al., 2018; Avalos et al., 2017; Yitshak-Sade et al., 2018; Bekkar et al., 2020). Most studies examine effects of short-term temperature (Avalos et al., 2017) or ambient temperature (Yitshak-Sade et al., 2018). Data from LMICs is sparse. For many LMICs, including those in equatorial or tropical climates, humid-heat exposures may be particularly health relevant (Bessah et al., 2022). Our group has developed temporally- and spatially-resolved humid-heat models that can be applied to extant cohorts in LMICs (Tuholske et al., 2021; Verdin et al., 2020). Wet bulb globe temperature (WBGT) is a heat measurement that measures heat stress more precisely in hot-humid environments (Budd, 2008). Shaded WBGT accounts for temperature, humidity, and wind speed to measure heat stress on an individual. Heat index (HI), is another widely-used heat stress metric that considers temperature and relative humidity (Bernard and Iheanacho, 2015).

To address these gaps, we leveraged the Ghana Randomized Air Pollution and Health Study (GRAPHS) cohort to examine time-varying associations between prenatal humid-heat exposures on birth outcomes. Specifically, we examined associations between maximum WBGT and HI, considered separately, on birth weight, length, and head circumference; and on incidence of small-for-gestational age, low birth weight, and preterm birth. First, we averaged exposures by trimester and employed linear regression to examine associations between trimester averaged humid-heat exposures and birth outcomes. Next, we employed distributed lag nonlinear models (DLNMs) to examine associations with humid-heat exposures and birth outcomes, to identify sensitive windows of exposure.

2. Methods

2.1. Participant characteristics

Participants were pregnant individuals enrolled in GRAPHS, a cluster randomized cookstove intervention trial previously described (Jack et al., 2015). Pregnant individuals were recruited between June 2013 and June 2015 from the Kintampo North Municipality and Kintampo South District of Ghana. Individuals were eligible for the study if they were pregnant with a singleton fetus at ≤ 24 weeks gestation confirmed by ultrasound (Boamah et al., 2014), were the primary cook in their household, and a non-smoker. Pregnancies were excluded from these analyses if delivery occurred before 28 weeks or if the birth anthropometrics was not measured within 72 h of birth. Participants were further excluded from analyses if they were missing covariates (age, body mass index, adequacy of prenatal visits, and examination of placental histopathology for malaria infection) resulting in a total of 1173 participants. All study procedures were approved by the Kintampo Health Research Centre (KHRC) Institutional Ethics Committee (IRB, 2017-31), the Ghana Health Service Ethics Review Committee, and Institutional Review Boards at Columbia University (IRB-AAAR4373) and Icahn School of Medicine at Mount Sinai (STUDY-17-01265). Informed consent was obtained for all pregnant individuals at study enrollment.

2.2. Modeling of wet-bulb globe temperature and heat index

We assigned each participant daily maximum WBGT and HI, beginning at the ultrasound-derived date of conception through the date of

delivery. Exposures were assigned at the given participant's community centroid. Community boundaries for our study region have been developed by our team using the "Open Buildings" public dataset of building footprints for the continent of Africa (Sirko et al., 2021; Open Buildings) Medgyesi et al., 2023). By applying a spatial clustering algorithm, we identified groups of buildings that form a community, drew boundaries along the perimeter, and then extracted the centroid of each community area. On average, study communities were 0.87 square kilometers.

As described in (Tuholske et al., 2021), daily maximum HI (HI_{max}) data was derived using CHIRTS-daily maximum air temperature (Verdin et al., 2020) and down-scaled daily minimum relative humidity estimates produced from ERA5 and MERRA-2 climate reanalysis data and CHIRTS-daily maximum air temperature (Tuholske et al., 2021), following the US National Weather Service procedure (NOAA). Daily maximum HI was then transformed to shaded WBGT using an established quadratic relationship that assumes fixed windspeeds (0.5 m/s) and no added influence from radiated heat (Eq. (1), Fig. 1 in 19). Shaded WBGT temperature, which has been used in heat epidemiological research (Pradhan et al., 2019), accounts for the combined non-linear effects of air temperature and atmospheric moisture on human physiology (Lemke and Kjellstrom, 2012). But because our estimation of WBGT does not account for solar radiation and assumes fixed wind speeds, the WBGT used here may be cooler, than actual in-situ WBGT. Radiated heat can add 2–3 °C to WBGT (Kjellstrom et al., 2013) and lower wind speeds will increase WBGT, whereas higher wind speeds have a neglectable effect on WBGT (Lemke and Kjellstrom, 2012).

$$\text{WBGT (}^{\circ}\text{C)} = -0.0034 \text{ HI}^2 \text{ (}^{\circ}\text{F)} + 0.095 \text{ HI (}^{\circ}\text{F)} - 34 \quad \text{Eq. 1}$$

Instead of using station data for Ghana, we use CHIRTS-daily and the two down-scaled reanalysis products to estimate WBGT for two reasons. First, only a handful of weather stations with a robust, longitudinal reporting record are available for Ghana (Verdin et al., 2020; Odoro et al., 2024). Second, CHIRTS-daily has been shown to be highly accurate compared to other gridded air temperature datasets for West Africa (Tuholske et al., 2021; Verdin et al., 2020). When validated against the quality-controlled station data available from NOAA's Climate Prediction Center for Accra, Ghana, the mean squared error (RSE) of CHIRTS-daily maximum air temperature 0.81 °C compared an RMSE of 1.80 °C (Verdin et al., 2020) of the Princeton Global Forcing dataset, another widely used air temperature dataset (Sheffield et al., 2006). Second, while gridded datasets like CHIRTS-daily, ERA5 and MERRA-2 have known biases for Ghana (Verdin et al., 2020; Sheffield et al., 2006) the 5-km WBGT estimates we utilize provide spatial coverage across Ghana's diverse local climates.

Daily maximum HI and WBGT over gestation were extracted for community centroids where participants lived, buffered by 5-km to account for possible edge effects. We use daily maximum WBGT (primary exposure) and HI (sensitivity exposure) because they capture the nonlinear effects of air temperature and humidity on human physiology (Baldwin et al.). We present our main findings using daily maximum WBGT (WBGT_{max}) to measure heat-stress because it is a widely used heat stress metric in epidemiologic research (Pradhan et al., 2019), follows the International Standards Organization's guidelines for occupational heat risk (Parsons, 2006), and is tied to physiological responses to heat stress (Budd, 2008).

2.3. Birth outcomes

Birth weight (g), birth length (cm), and head circumference (cm) were measured by community-based field workers as previously described (Quinn et al., 2021). Birth weight was measured to the nearest 10 g using Tanita BD 585 digital baby scale (Tokyo, Japan) and both birth length and head circumference were measured to the nearest 0.1 cm using the Ayrton Infantometer Model M-200 (Ayrton Corp, MN,

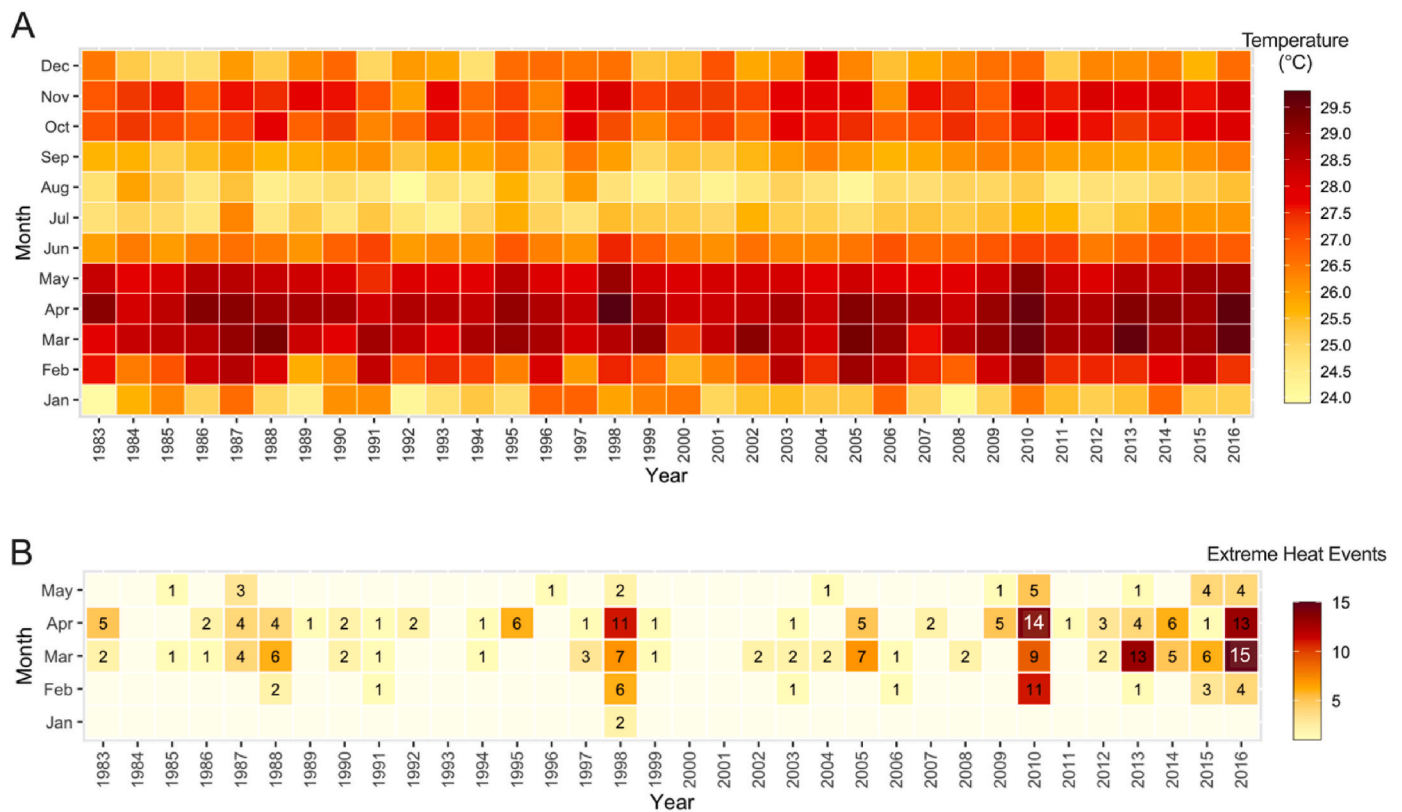


Fig. 1. Monthly maximum wet-bulb globe temperature (A) and total number of extreme heat events (WBGTmax >30 °C) (B) averaged across GRAPHS study communities from 1983 to 2016.

USA) and a Lasso-oTM (Child Growth Foundation, UK), respectively. Gestational age at delivery was measured using ultrasound estimates from enrollment as previously described (Boamah et al., 2014). Preterm birth (PTB) was defined as delivery before 37 weeks gestation. Low birth weight (LBW) was defined as less than 2500 g and small for gestational age (SGA) was defined as less than 10th percentile weight and was calculated based on a Ghanaian specific growth curve (Quinn et al., 2021).

2.4. Covariate selection

Covariates were selected *a priori* based on research that identified them as key factors associated with temperature or birth outcomes. Multivariable models adjusted for enrollment maternal age (in years), maternal body mass index (in kg/m²), parity (nulliparous/multiparous), and ethnicity (categorical variable with four levels); number of prenatal visits (4 or more visits/less than 4 visits); infant sex (male/female); placental malaria (yes/no; determined by placental histopathology with both acute and chronic infections suggesting prenatal infection (Asante et al., 2013)); and season of birth (dry [November–March]/wet [April–October]).

2.5. Statistical analysis

We first averaged and visualized WBGTmax across all GRAPHS study communities for the period of available data (1983–2016) to identify trends in WBGTmax. We then tabulated the number of extreme heat events, defined as having a WBGTmax of >30 °C following International Standards Organization thresholds for occupational risk from dangerous humid-heat (ISO, 2017), each year over this period.

We examined associations between trimester average WBGTmax (1st trimester, 1–97 days; 2nd trimester, 98–188 days; 3rd trimester, 189–280 days gestation) and pregnancy average WBGTmax and birth

outcomes, considered separately. In multivariable linear regression models, we included all three trimester WBGTmax averages in the same model to understand associations between trimester-specific humid-heat exposure independent of other trimester exposures on birth weight, length and head circumference and adjusted for covariates above. We performed multivariable logistic regression as above to examine associations with PTB, LBW and SGA.

Next, we employed distributed lag nonlinear models (DLNMs) to examine time-varying associations between WBGTmax and birth outcomes (except preterm birth), considered separately. The DLNM framework allows for a nonlinear relationship and estimates time-varying associations between humid-heat exposure and birth outcomes (Gasparrini, 2014). We assigned WBGTmax from the ultrasound-estimated date of conception (pregnancy start date) through delivery. We truncated daily exposure data to the end of 37 weeks gestation to derive a dataset of equal length for all participants. We did not derive exposure data through 40 weeks gestation, as it generated different sensitive windows in late gestation that may be an artifact of the imputation process. Given this approach, we did not investigate time-varying associations with PTB. A natural cubic spline was used for the nonlinear effect for both temperature and lag, and the degree of freedom with the lowest BIC was selected for each model (Table S1). The median WBGTmax rounded to the nearest one degree (27 °C) was defined as the reference value. Associations at the 25th percentile (first quartile) and 75th percentile (third quartile) WBGTmax in relation to the reference value were reported. A statistically significant sensitive window was identified when the 95% confidence bands did not contain zero.

To account for uncertainty around the best measure of health-relevant humid heat (Baldwin et al., 2023), we performed sensitivity analyses to examine associations between H_{lmax} and birth outcomes using the strategies above. For H_{lmax} DLNMs, the median H_{lmax} rounded to the nearest degree (37 °C) was used as the referent. DLNMs

were implemented using the *dlm* package in R (Gasparrini, 2014). We had 18 infants that were stillbirth and acknowledge their birth measurements may be inexact given the potential interval from *in utero* death until delivery for some stillbirths. We therefore performed sensitivity analyses excluding stillbirth participants.

3. Results

3.1. Study population characteristics

Fig. S1 outlines participant recruitment, inclusion/exclusion criteria, and the final sample size. Table 1 describes the characteristics of our study population. Our population (N = 1173) had a mean age of 28 ± 7.2 years and individuals in the study were primarily multiparous (83%) and attended four or more antenatal visits (70%). Fifty percent of the newborns were female, and the overall population had an average birth weight of 2890 g, birth length of 46.5 cm, head circumference of 33.5 cm, and gestational age of 39.5 weeks. Twenty-two percent of the newborns measured SGA, 17% were LBW and 4% were PTB. The births were relatively evenly distributed across the different months throughout the year with a larger proportion (61%) being born in the wet season (April to October).

3.2. Historical wet bulb globe temperature in study region

Fig. 1 depicts the average monthly WBGTmax (A) and number of extreme heat events (B), defined as the number of days per year WBGTmax >30 °C, from 1983 to 2016 in the Kintampo North Municipality and Kintampo South District of Ghana. We observe the typically warmer months (Feb–May) becoming hotter and the cooler months

Table 1

Descriptive characteristics of the pregnant women, birth outcomes and anthropometry of newborns in the GRAPHS cohort (N = 1173).

Maternal Characteristics	N	Mean ± SD or %
Ethnicity ^a , N (%)		
1	198	17
2	148	13
3	776	66
4	51	4
Parity (N, %)		
Nulliparous	204	17
Multiparous	969	83
Number of antenatal visits (N, %)		
<4	352	30
≥4	821	70
Placental Malaria Status (N, %) ^b		
Negative	884	75
Positive	289	25
Maternal Age (years)	1173	28 ± 7.2
Maternal BMI (kg/m ²)	1173	23 ± 3.2
Birth Outcomes ^c	N	Mean ± SD or %
Infant Sex		
Female	583	50%
Male	590	50%
Birth Weight (g)	1169	2890 ± 457
Birth Length (cm)	1156	46.5 ± 3.6
Head Circumference (cm)	1143	33.5 ± 2.4
Gestational Age (weeks)	1173	39.2 ± 1.7
Small for Gestational Age	257	22%
Low Birth Weight	194	17%
Preterm Birth	49	4%
Stillbirth	18	2%
Season of Birth		
Wet	714	61%
Dry	459	39%

^a Ethnicity information is labelled numerically due to privacy concerns.

^b Placental malaria determined by placental histopathology.

^c Two participants were missing birth weight, birth length, and head circumference.

(Aug–Oct) becoming less cool over the past three decades. We see a statistically significant increase in WBGTmax and HImax over the years (Fig. S2). Additionally, we also see higher incidences of extreme heat events especially beginning in the early 2000s.

Distribution of weekly temperatures remained relatively consistent over gestation (Fig. S3). Weekly WBGTmax exposures ranged from 22.7 °C to 30.8 °C and HImax ranged from 29.0 °C to 44.3 °C. The mean WBGTmax was 27.0 °C ± 1.1 for the first trimester, 27.2 °C ± 0.96 for trimester 2, 27.3 °C ± 1.1 for trimester 3, and 27.2 °C ± 0.51 for the overall pregnancy. The median WBGTmax was 27 °C, 27.1 °C, and 27.2 °C for the first, second, and third trimester respectively and 27.2 °C for the overall temperature. The average number of extreme heat events experienced in each trimester was 4.1 ± 8.6 for the first trimester, 4.2 ± 8.1 for second trimester, 4.8 ± 8.6 for the third trimester, and 13.1 ± 13.7 for overall pregnancy, with 82% of the population experiencing at least one extreme heat event throughout the pregnancy (Table S2).

3.3. Associations between trimester average WBGTmax and birth outcomes

Higher average WBGTmax over pregnancy was associated with a higher head circumference ($\beta = 0.47$ cm, 95% CI: 0.16, 0.79 per 1° increase in WBGTmax) (Fig. 2C). We also observed that higher average WBGTmax in the first ($\beta = 0.16$ cm, 95% CI: 0.02, 0.29 per 1° increase in WBGTmax) and third ($\beta = 0.17$ cm, 95% CI: 0.02, 0.32 per 1° increase in WBGTmax) trimester were associated with a higher head circumference (Fig. 2C). Additionally, higher average WBGTmax in the second trimester was associated with lower birth weight ($\beta = -36.5$ g, 95% CI: -72.9, -0.2) and birth length ($\beta = -0.32$ cm, 95% CI: -0.61, -0.02) per 1° increase in average WBGTmax (Fig. 2A and B). Higher average WBGTmax in the second trimester was also associated with higher incidence of pre-term birth ($\beta = 1.53$, 95% CI: 1.00, 2.35) per 1° increase (Fig. 2F).

Sensitivity analyses using heat index as the exposure of interest found similar results where higher head circumference was associated with higher HImax in the first ($\beta = 0.08$ cm, 95% CI: 0.01, 0.15) and third ($\beta = 0.09$ cm, 95% CI: 0.01, 0.17) trimester and over pregnancy ($\beta = 0.25$ cm, 95% CI: 0.08, 0.41) per 1° increase in HImax (Fig. S4). Similar to the WBGTmax results, higher average HImax in the second trimester was associated with lower birth length ($\beta = -0.17$ cm, 95% CI: -0.32, -0.01) per 1° increase in HImax (Fig. S4). A trend was identified between higher average HImax in the second trimester and lower birth weight ($\beta = -18.4$ g, 95% CI: -37.3, 0.5) per 1° increase in HImax, (Fig. S4)

3.4. Time-varying associations between prenatal WBGTmax and birth outcomes

AIC and BICs from tuning parameters for all models are reported in Table S1. Final models used a degree of freedom of 4 for both the temperature and lag variables for both WBGTmax and HImax.

Fig. 3 shows the associations with WBGTmax and birth weight. DLNMs identified a sensitive window from 22 to 129 days of gestation where WBGTmax at 26 °C (25th percentile) was associated with higher birth weight as compared to 27 °C (median). No association was identified between WBGTmax at the 75th percentile (29 °C) as compared to the median. We also observed that lower WBGTmax (26 °C; 25th percentile) was associated with longer birth length, as compared to 27 °C. Specifically, we identified a sensitive window of 17–120 days gestation for 26 °C vs 27 °C. At 29 °C, however, we did not identify an association with birth length, as compared to 27 °C. For head circumference, we observed sensitive windows from 104 to 257 days, where WBGTmax of 26 °C was associated with a smaller head circumference and sensitive windows from 21 to 167 and 194–259 days where WBGTmax of 29 °C was associated with a larger head circumference, compared to 27 °C.

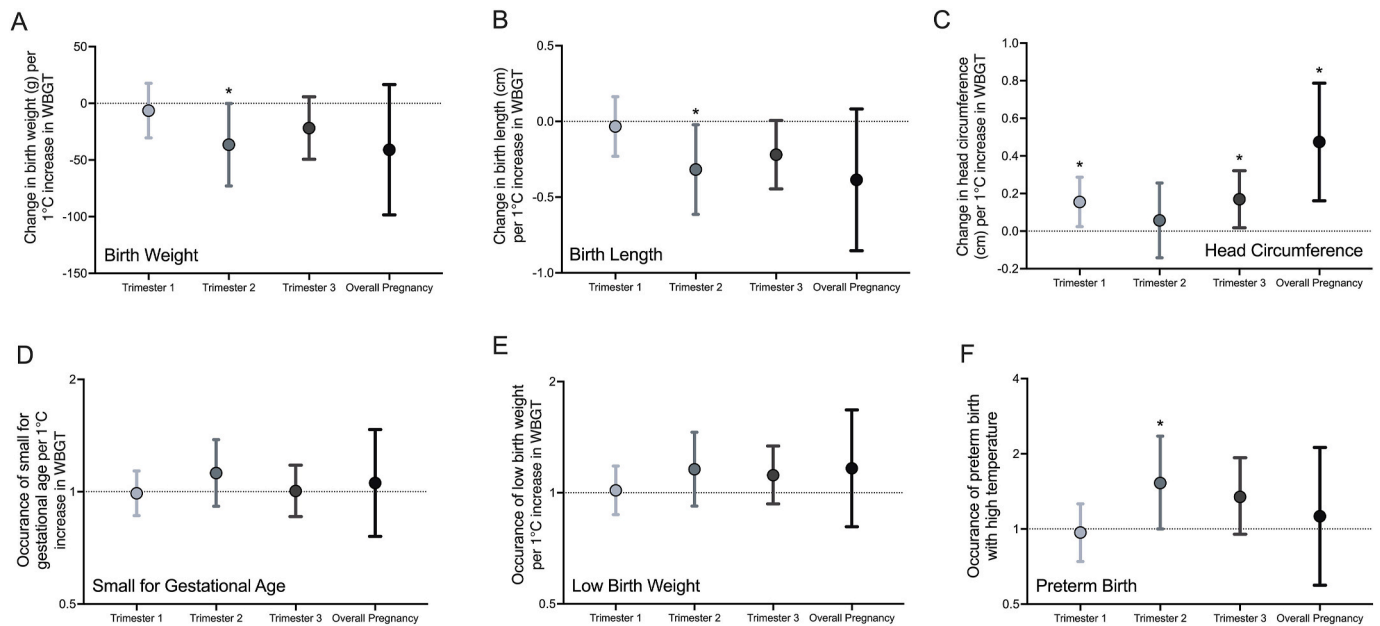


Fig. 2. Effect estimates from multivariable regression models examining the associations of WBGTmax over pregnancy on birth outcomes. Error bars around effect estimates represent 95% confidence intervals. All models were adjusted for maternal age, BMI, parity, ethnicity, adequacy of prenatal visits, infant sex, placental malaria, and season of birth.

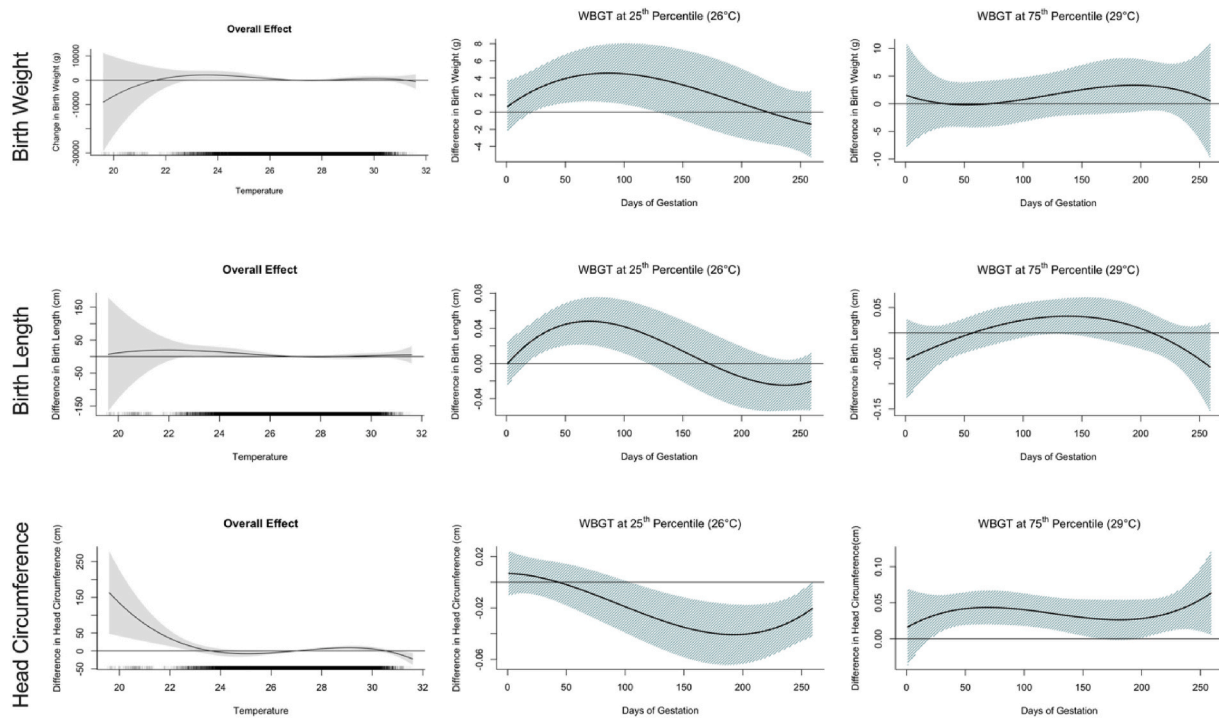


Fig. 3. The overall effect of daily maximum WBGT on birth weight, birth length and head circumference, and the difference in temperature at the 25th (26 °C) and 75th (29 °C) percentile across days of gestation. Shaded areas represent 95% confidence intervals. All models were adjusted for maternal age, BMI, parity, ethnicity, adequacy of prenatal visits, infant sex, placental malaria, and season of birth.

Fig. 4 reports the odds ratios of categorical birth outcomes (low birth weight and small for gestational age) across gestation. We observed lower odds of low birth weight with sensitive windows at 172–196 at 26 °C vs 27 °C (Fig. 4). Additionally, we observed lower odds of small for gestational age with sensitive windows at 22–208 at 26 °C and 1–11 and 154–232 at 29 °C compared to 27 °C (Fig. 4).

3.5. Associations between heat index and birth outcomes

As a sensitivity analysis, we examined lag-response relationships with gestational HImax exposures and birth outcomes (Figs. S5 and S6). We identified similar sensitive windows to WBGTmax where HImax at the 25th percentile (34 °C) was associated with a higher birth weight and birth length and lower head circumferences and HImax at the 75th percentile (39 °C) was associated with higher head circumference

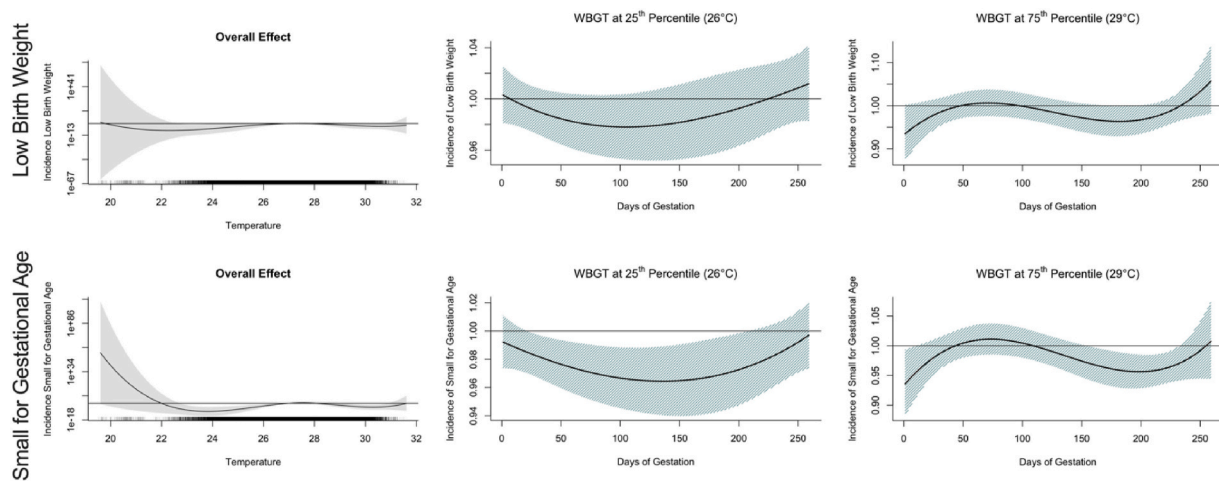


Fig. 4. The overall effect of daily maximum WBGT on incidence of low birth weight and small for gestational age and odds ratios for temperature at the 25th (26 °C) and 75th (29 °C) percentile across days of gestation. Shaded areas represent 95% confidence intervals. All models were adjusted for maternal age, BMI, parity, ethnicity, adequacy of prenatal visits, infant sex, placental malaria, and season of birth.

compared to 37 °C. Additionally, we also identified lower birth length at 206–250 days of gestation at 34 °C compared to 37 °C. At 39 °C, we identified lower birth length at 4–14 and 229–251 days of gestation and higher birth length at 99–137 days of gestations compared to 37 °C (Fig. S5).

We did not identify an association between HImax across gestation and LBW. However, odds for SGA were lower between 23 and 160 days at 34 °C and 149–231 at 39 °C compared to 37 °C (Fig. S6).

3.6. Additional sensitivity analysis

The removal of stillbirth participants also had no meaningful impact on the association between WBGTmax and birth outcomes (Table S3)

4. Discussion

Our analysis identified that our study area in Ghana has experienced a trend in increased humid-heat exposures between 1983 and 2016. Cohort analyses, both by trimester averages and DLNMs, find that higher humid-heat exposures over pregnancy were associated with worse birth outcomes. Specifically, trimester averages identified that higher WBGTmax in the second trimester were associated with decreased birth weight and birth length, as well as a higher incidence of pre-term birth. Utilizing DLNMs, we identified time-varying associations over pregnancy such that lower WBGTmax was associated with longer, or improved, birth length and higher birth weight, as compared to median WBGTmax. Sensitivity analyses similarly found that higher HImax is associated with shorter birth length as compared to median HImax. Taken together, these data support a negative health impact of humid-heat exposures over gestation. Given the importance of birth outcomes and newborn size on lifelong health, these data support the need for longer-term follow-up of the cohort to understand how humid-heat exposures over pregnancy may influence life course health.

Literature examining associations with temperature during gestation and birth outcomes is mostly focused on preterm birth, low birth weight, and stillbirth; predominantly evaluates populations in high income countries and focuses on short-term and ambient temperature exposures. In our study, we observed that WBGTmax at the 25th percentile was associated with longer birth length, higher birth weight, and lower incidence of SGA at specific windows, suggesting that having a lower temperature may have a protective effect on birth size. Other studies have reported associations between higher temperature across pregnancy in the Northeast US and higher risk of term SGA (Sun et al., 2019). Furthermore, both extreme hot and cold temperatures were associated

with increased odds of SGA in China (Li et al., 2023). Similar to our results that reported the end of the first trimester and beginning of the second trimester as a sensitive windows, these studies identified the second trimester as an important window of exposure for fetal growth (Sun et al., 2019; Li et al., 2023).

Contrary to our results, the limited research examining associations with temperature and birth length has reported that colder temperatures are associated with lower birth lengths (Rashid et al., 2017; Andalón et al., 2016; Bruckner et al., 2014). The conflicting results are most likely due to the range of temperatures that are being examined in our study compared to these other studies. When examining sensitive windows of exposure, cold shocks during the first and second trimester were associated with a lower birth length (Andalón et al., 2016), suggesting a similar window of sensitivity to our study. The variations among the windows of sensitivity between the different studies can be attributed to the difference in temperature ranges as well as the meteorological differences in the various climate zones being examined (Zhang et al., 2017).

There is no consensus on how temperature may affect birth outcomes. There are several hypotheses that suggest that higher temperature may cause a reduction in placental blood flow, increase production of heat shock proteins, or initiate an inflammatory response that may trigger preterm birth (Samuels et al., 2022; Fukushima et al., 2005). Higher temperature is also associated with other pregnancy complications such as gestational diabetes, pre-eclampsia – risk factors for preterm birth (Samuels et al., 2022) (Pace et al., 2021; Shashar et al., 2020; Bonell et al., 2022). More research is needed to fully understand these mechanisms.

Birth outcomes are important indicators of future health, and specifically, studies have reported that infants born at earlier gestational ages are more likely to have increased risk of cardiovascular, metabolic, respiratory, neurodevelopment, and kidney diseases (Pravia and Benny, 2020; Crump, 2020). Additionally, infants born smaller have an increased risk of cardiovascular disease, obesity, type 2 diabetes, and increased risk of hospitalizations later in life (Saenger et al., 2007; Mehl et al., 2022). As infants are already more likely to be born sooner and lighter in low- and middle-income countries (Bauserman et al., 2020), it is important to characterize potential associations with temperature and mitigate further adverse birth outcomes.

We employed two complementary strategies to examine associations between humid heat exposure over pregnancy and birth outcomes. First, we used trimester averages in a linear regression framework to understand the magnitude of effect in each trimester and over gestation. Second, we employed the DLNM framework to examine time-varying

associations and to identify windows of susceptibility. In most studies examining temperature and birth outcomes, temperature is averaged over the entire pregnancy or over trimesters and therefore may miss important windows that are not constrained by the time points (Wilson et al., 2017). However, the use of DLNMs allow for a joint assessment of multiple short intervals of exposure over the pregnancy, allowing us to reduce the bias and account for the potential nonlinear associations between temperature and birth outcomes (Gasparrini, 2014). Furthermore, we also examined associations of birth outcomes with a health-relevant temperature measure, WBGT (Pradhan et al., 2019), that considers the combined effects of temperature and humidity on human physiology. We note that our method to calculate WBGT is a quadratic transformation of HI (Bernard and Iheanacho, 2015), and therefore diminishes the influence of extreme HI values (Fig. 4 in 16, 26). We also note there is a divergence in the evidence between physiological and epidemiological on the degree to which humidity impacts health responses to heat (Baldwin et al.). This study was also conducted in a global south population, which may have different susceptibilities than global north populations (Green et al., 2019; Levy and Patz, 2015).

A limitation of this study is that Ghana is a low-latitude tropical climate and therefore we are unable to examine the effects of cooler (or warmer) temperature extremes, limiting the generalizability to populations in other climates zones. Further, we calculate shaded WBGTmax that assumes fixed wind speeds (0.5 m/s) and as such our estimation of WBGT may under-estimate WBGT sunny days or at locations with less air movement (Lemke and Kjellstrom, 2012; Kjellstrom et al., 2013). Lastly, although we adjusted for several relevant confounders in our analyses, our associations may be affected by other variables such as maternal diet, lifestyle factors, or pollutant exposures.

5. Conclusion

In conclusion, we found that consistent evidence across models that higher humid-heat exposure in mid-gestation were associated with worse outcomes, including lower birth weight, shorter birth length and higher incidence of small for gestational age and pre-term birth, as compared to the median temperature. This study is one of the few examining critical windows of exposure to temperature in relation to birth outcomes in the global south. Given the rising levels of temperature worldwide, and the disproportionate burden on persons living in the global south, our study highlights the urgency to develop adaptation strategy and preserve life course health.

CRedit authorship contribution statement

Aalekhya Reddam: Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Conceptualization. **Mohammed Nuhu Mujtaba:** Writing – review & editing, Project administration, Methodology. **Cascade Tuholske:** Writing – review & editing, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Seyram Kaali:** Writing – review & editing, Project administration, Investigation. **Kenneth Ayuurebobi Ae-Ngibise:** Writing – review & editing, Project administration, Investigation. **Blair J. Wylie:** Writing – review & editing, Supervision. **Danielle N. Medgyesi:** Writing – review & editing, Methodology. **Ellen Boamah-Kaali:** Writing – review & editing, Project administration, Investigation. **Andrea A. Baccarelli:** Writing – review & editing, Supervision, Funding acquisition. **Oscar Agyei:** Writing – review & editing, Project administration, Investigation. **Steve N. Chillrud:** Writing – review & editing, Project administration, Investigation. **Kwaku Poku Asante:** Writing – review & editing, Supervision, Project administration, Investigation, Funding acquisition. **Darby W. Jack:** Writing – review & editing, Supervision, Resources, Project administration, Investigation, Funding acquisition, Conceptualization. **Alison G. Lee:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Investigation, Funding acquisition, Formal analysis,

Conceptualization. **Sulemana Watara Abubakari:** Writing – review & editing, Project administration, Investigation.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2024.120557>.

Data availability

The data that has been used is confidential.

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